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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,674	02/28/2002	Johannes Bartholomacus	148/50986	2545

23911 7590 11/17/2003

CROWELL & MORING LLP
INTELLECTUAL PROPERTY GROUP
P.O. BOX 14300
WASHINGTON, DC 20044-4300

EXAMINER	
PULLIAM, AMY E	

ART UNIT	PAPER NUMBER
1615	6

DATE MAILED: 11/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/084,674	Applicant(s) BARTHOLOMAEUS ET AL.	
	Examiner Amy E Pulliam	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11,12,15,17,18,21,30-32,55-58 and 62-67* is/are pending in the application.

4a) Of the above claim(s) *10,13,14,16,19,20,22-29,33-54 and 59-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11,12,15,17,18,21,30-32,55-58 and 62-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt of Papers

Receipt is acknowledged of the Extension of Time and the Election of Species, both received by the Office July 21, 2003.

Election/Restrictions

Applicant's election, without traverse, in paper number 5, is acknowledged. The examiner accepts Applicant's listing of the applicable claims, except for one small change. It is the position of the examiner that claims 50-54 do not read on the elected species, and these claims have therefore have been withdrawn and not examined on the merits. The election of species is made final. Claims 1-9, 11, 12, 15, 17, 18, 21, 30-32, 55-58, and 62-67 are currently pending.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the active agents tramadol and promethazine, does not reasonably provide enablement for any salt forming pharmaceutical active agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404, where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant has presented the claims very broadly, reciting "salt forming active ingredient" in general, and claiming a laundry list of many types of pharmaceutically active agents. Upon careful examination of the specification, the Examiner notes that the examples pertain only to tramadol and promethazine. Applicants have provided no discussion or explanation regarding the use of their invention with respect to all other known, salt-forming, pharmaceutically active agents. Applicant makes a broad statement at the conclusion of the specification, stating "[t]he foregoing description and examples have been set forth merely to illustrate the invention and are not intended to be limiting. Since modifications of the described embodiments incorporating the spirit and substance

of the invention my occur to persons skilled in the art, the invention should be construed broadly to include all variations falling within the scope of the appended claims and equivalents thereof." The Examiner does not find this broad, catch all phrase to be enabling for the scope of the instant claims.

Applicant fails to provide information allowing the skilled artisan to ascertain the instant invention, as claimed, without undue experimentation. As discussed above, in the instant case, the specification gives guidance for only two compounds: tramadol and promethazine. Absent additional guidance, the specification therefore fails to provide sufficient working examples. It is noted that the wide range of active compounds claimed, for instance in claims 5 and 8, cover extremely different compounds, structurally and physiologicallyClaims 1-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the active agents tramadol and promethazine, does not reasonably provide enablement for any salt forming pharmaceutical active agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404, where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant has presented the claims very broadly, reciting "active agent" in general, and using a laundry list of many types of pharmaceutically active agents. Upon careful examination of the specification, the Examiner notes that the examples pertain only to tramadol and promethazine. Applicant's have provided no discussion or explanation regarding the use of their invention with respect to all other known pharmaceutically active agents. Applicant makes a broad statement at the conclusion of the specification, stating "[t]he foregoing description and examples have been set forth merely to illustrate the invention and are not intended to be limiting. Since modifications of the described embodiments incorporating the spirit and substance of the invention my occur to persons skilled in the art, the invention should be construed broadly to include all variations falling within the scope of the appended claims and equivalents thereof." The Examiner does not find this broad, catch all phrase to be enabling for the scope of the instant claims.

Applicant fails to provide information allowing the skilled artisan to ascertain the instant invention, as claimed, without undue experimentation. As discussed above, in the instant case, the specification gives guidance for only two compounds: tramadol and

promethazine. Absent additional guidance, the specification therefore fails to provide sufficient working examples. It is noted that the wide range of active compounds claimed, for instance in claims 5 and 8, cover extremely different compounds. Given the unpredictability of the pharmaceutical art, it is known that different active agents may respond uniquely in different formulations, therefore requiring each embodiment (or at least each class of compounds or structures) to be individually assessed for physiological activity. The instant claims read on all pharmaceutically active agents, therefore necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. For each of the above reasons, Applicants fail to provide sufficient information or guidance necessary to practice the invention as claimed, absent a great deal of undue experimentation.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are both unclear for the following reason. Claim 1 requires an active ingredient present as at least two different salts in a solid aggregation state. However, both claim 11 and 12 discuss "the active ingredient salt" a if the formulation requires only one salt form. This is in contradiction to the language of claim 1. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-9, 11, 12, 15, 17, 18, 21, 30-32, 55-58, and 62-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/01111 to Oshlack *et al.*.

Oshlack *et al.* disclose a stabilized sustained release oral solid dosage form which includes an effective amount of tramadol or a pharmaceutically acceptable salt thereof, dispersed in a material of a hydrophobic material (abstract). Oshlack *et al.* teach that suitable pharmaceutically acceptable salts of tramadol for use according to the present invention are those conventionally known in the art, such as pharmaceutically acceptable acid addition salts (page 11, lines 3-5). Although tramadol hydrochloride is specifically mentioned, the reference suggests the use of others, or tramadol HCl would be the only salt discussed throughout the specification. Oshlack *et al.* also teach that the sustained release matrix includes a hydrophobic polymer which comprises one or more

alkylcelluloses, especially ethylcellulose (page 15, lines 13-16). Additionally, the reference teaches that the sustained release preparation can be presented as granules, multiparticulates, capsules, or tablets, with tablets being preferred (page 17, lines 22-23). Furthermore, said tablets may be coated with a film coating, such as a hydrophobic polymer, for example, an acrylic polymer, including but not limited to acrylic acid and methacrylic acid copolymers (page 18, lines 14-17).

Although Oshlack *et al.* do not teach each and every tramadol salt, as discussed above, the reference does suggest the existence and the use of other well known tramadol salts. Absent evidence to the contrary, one of ordinary skill in the art would have been motivated to use any known salt of tramadol in the disclosed invention.

Furthermore, although Oshlack *et al.* do not specifically teach the particular enteric coating claimed by Applicant, the reference does suggest the use of film coatings in general. Additionally, the reference teaches the use of acrylic/ methacrylic copolymers, some of which are known to be enteric. Absent evidence to the contrary, it is unclear what unexpected result the addition of a particular enteric coating adds to the invention. The selection of a known material based on its suitability for its intended use is obvious absent a clear showing of unexpected results attributable to the Applicant's specific selection.

Also, Oshlack *et al.* do not specifically teach that the different salt forms of tramadol will have differing rates of release. However, the rate of release of a particular form of an active is a property which is inherent and characteristic to that particular form. Absent some unusual combination, or some showing of unexpected results, the rates of

release of the differing salt forms are not found to render patentable distinction to the claims, as this is a property which is characteristic to the drug form.

Therefore, Oshlack *et al.* teach a sustained release, oral, tablet formulation comprising tramadol or one of the pharmaceutically acceptable salts thereof. Furthermore, the formulation comprises ethylcellulose as a matrix excipient and may include an enteric film coating, such as an acrylic/ methacrylic copolymer. As stated in *In Re Kerkhoven*, 205 USPQ 1069, 1072 (CCPA- 1980), "It is prima facie obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. As this court explained in Crockett, 126 USPQ 186, 188 (CCPA- 1960), the idea of combining them flows logically from their having been individually taught in the prior art. As shown by the teachings of Oshlack *et al.*, tramadol and its pharmaceutically acceptable salts are known to shown to be useful for the same purpose: to treat pain (page 4, line 7). Oshlack *et al.* can therefore be interpreted as teaching several different formulations useful for the same purpose ((1) formulation comprising tramadol, (2) formulation comprising tramadol HCl, (3) formulation comprising another known tramadol salt). Therefore, as taught by *In Re Kerkohven*, one skilled in the art would have been motivated to combine two or more of these formulations, to create a third formulation which would also be useful for the treatment of pain. Therefore, this invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E Pulliam whose telephone number is 703-308-4710. The examiner can normally be reached on Mon-Thurs 7:30-5:00, Alternate Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

A. Pulliam
Patent Examiner
Art Unit 1615
November 12, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600